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10/723,365

11/26/2003

Dirk van den Boom

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EXAMINER

WOOLWINE, SAMUEL C

ART UNIT

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1637

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/723,365	Applicant(s) BOOM ET AL.	
	Examiner SAMUEL WOOLWINE	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 74-127, 129-131, 140, 158, 162, 164 and 169-173 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 74-127, 129-131, 140, 158, 162, 164 and 169-173 is/are rejected.
- 7) ☒ Claim(s) 76, 99, 106, 116 and 131 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>06/25/2009; 08/11/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status

Applicant's reply filed 05/07/2009 is acknowledged. Claims 74-127, 129-131, 140, 158, 162, 164, and 169-173 are pending (claims 169-173 are new). Any previous rejection over a claim that is no longer pending is withdrawn as moot.

The rejection under 35 USC 101 made in the Office action mailed 12/08/2008 is withdrawn in view of amendment to independent claims 74, 115, 124, 129 to recite that mass signals are generated by mass spectrometry, thereby meeting the "machine-or-transformation" test set forth in *In re Bilski*, 88 USPQ2d 1385 (Fed. Cir. 2008) (a mass spectrometer is a particular machine). However, this amendment does raise some objections and new issues under 112, 2nd paragraph as discussed below for some dependent claims.

The rejection of claims 74-108, 112-114, 124-127, 129-131, 140 and 158 under 35 USC 112, 2nd paragraph (omission of essential method steps) made in the Office action mailed 12/08/2008 is withdrawn for one reason only, the reason being that the rejection was made under the wrong paragraph of 35 USC 112. The rejection *should* have been made, and now is made, under 35 USC 112, 1st paragraph. The separate issue under 112, 2nd paragraph, for claims 124-128 regarding "amino acids" has been resolved by Applicant's amendment. Applicant's other arguments, which would still apply to the rejection under 112, 1st paragraph, will be addressed following the rejection.

New objections and grounds of rejection are set forth below, not all of which are necessitated by amendment. This action is NON-FINAL.

Claim Objections

Claim 106 is objected to because of the following informalities: there is an inadvertent marking: "candidate_sequences" should be "candidate sequences". Appropriate correction is required.

Claims 76, 99, 116 and 131 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Each of these dependent claims recites "wherein the mass signals are determined [or generated] by mass spectrometry". However, independent claims 74, 115, 124 and 129 have been amended to recite that the mass signals are generated by mass spectrometry. Therefore, claims 76, 99, 116 and 131 are not further limiting.

Claim Interpretation

Although the following claim interpretation was already stated in the previous Office action, it bears repeating here. Claim 74 recites a method for "determining the sequence in one or more sequence variations in a target nucleic acid". The examiner construes this to mean just what it says, i.e. determining the sequence variation, not just that a variation is present. Claim 74 also recites "one specific cleavage", which the examiner construes as foreclosing any additional specific cleavage reactions. It is noted that dependent claim 91, for example, recites "wherein two or more specific cleavage agents are utilized to generate fragments". This is not necessarily inconsistent with the "one specific cleavage" recited in claim 74, so long as both agents

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are used together in the same reaction. For example, cleaving a target nucleic acid in a reaction comprising a C-specific agent and a G-specific agent would produce "one specific cleavage".

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 74-108, 112-114, 124-127, 129-131, 140 and 158 are rejected under 35 U.S.C. 112, first paragraph, as omitting a scoring step critical or essential to the practice of the invention. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976) and MPEP 2172.01.

Claim 74, step (d) recites "identifying a reduced set of candidate sequence variations corresponding to the compomer witnesses, whereby the one or more sequence variations in the target nucleic acid are determined from the candidate sequence variations". Similarly, claims 124 and 129 recite determining the sequence variation(s) from the candidate sequence variations [the algorithms in these claims being used to generate the set of *candidate* sequence variations]. In other words, after the set of candidate sequence variations (i.e. the list of *possible* sequences) is generated, the *actual* sequence of the variation(s) is determined. There is a gap in the method; how does one go from this list of possible sequences to the actual sequence? The only means taught in the disclosure that the examiner found was through the step of scoring the candidate sequences (for example, figure 1; paragraph [0027] of

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published application: "The value of the scores...can then be used to determine the sequence variation candidate that corresponds to the actual target nucleic acid sequence."). This is in fact recited in dependent claims 109 and 162, and it is recommended to incorporate such limitations into the independent claims (74, 124, 129) to obviate the rejection.

Claim 97 is rejected under this section on additional, and new, grounds. One of the types of nucleic acid recited in claim 97 is PNA (peptide nucleic acid). The examiner does not see anything in the disclosure teaching how to specifically cleave PNA (as would be required by claims 74 and 85, from which claim 97 depends). PNA would not, for example, be susceptible to cleaving by restriction endonucleases or RNases. Furthermore, Applicant has taught no specific chemical cleavage process for PNA.

Response to Arguments

Applicant's arguments filed 05/07/2009 have been fully considered but they are not persuasive.

Applicant argues:

It is respectfully submitted that claim 74 is clear without a scoring step. The specification discusses using algorithms for various steps of the claimed method, one of which is uses the value of scores "to determine the sequence variation candidate that corresponds to the actual target nucleic acid sequence," paragraph 0027. One of skill in the art at the time of filing of the instant application can recognize several different ways to use algorithms in performing various steps of a method including the step of claims 74, 124 and 129 "whereby one or more sequence variations in the target nucleic acid are determined from the candidate sequence variations."

This argument is not persuasive. The issue is not that the claims lack clarity. The issue is also not that the specification fails to disclose how to use algorithms to score the sequence variation candidates. The issue is that such scoring is an essential step, and therefore must be recited in the claim; see MPEP 2172.01:

"A feature which is taught as critical in a specification and is not recited in the claims should result in a rejection of such claim under the enablement provision section of 35 U.S.C. 112. See *In re Mayhew*, 527 F.2d 1229, 1233, 188 USPQ 356, 358 (CCPA 1976). In determining whether an unclaimed feature is critical, the entire disclosure must be considered. Features which are merely preferred are not to be considered critical. *In re Goffe*, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976)."

In *Mayhew*, the court affirmed a rejection based on the failure of the claims to recite a "cooling zone" as well as the location thereof (both of which elements were, however, disclosed in the specification).

Here, as in *Mayhew*, the issue is not that the specification did not disclose the essential element, but that it is not recited in the claims.

It is self-evident that merely "identifying a reduced set of *candidate* sequence variations corresponding to the compomer witnesses" does not, in and of itself, *determine* the sequence variation. Hence, a step of scoring the set of *candidate* sequence variation, as disclosed in the specification, would be essential.

Applicant argues:

The instant application notes that methods may include using a score "to determine the sequence variation candidate that corresponds to the actual target sequence," paragraph 0125. However, other algorithms may also be used. For example, paragraph 0043 discusses use of algorithms in general: "analysis of these signals by using algorithms that screen the signals to select only those that are likely to represent true sequence variations within the target nucleic acid."

Evidently, Applicant is averse to the word "scoring". However, regardless of the terminology employed, there must be some operation performed on the reduced set of sequence variation candidates to ultimately arrive at the actual sequence variation, whether it is called "scoring" or something equivalent thereto.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 81, 100, 101 and 169-173 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 81 recites the limitation "wherein the polymorphism" in reference to claim 74. There is insufficient antecedent basis for this limitation in the claim, as claim 74

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does not recite any "polymorphism". It would appear claim 81 should depend from claim 79, which recites that the sequence variation is a mutation or a polymorphism.

Claims 100 and 101 are rejected under this section for different reason.

Applicant has amended claim 74, upon which claims 100 and 101 depend, to recite that mass signals are generated for the target and reference nucleic acid fragments by mass spectrometry. It is unclear how one would determine the mass signal of a "simulated fragment" using a mass spectrometer. One could simulate fragmentation of a sequence on a computer, or with pencil and paper. But the independent claims clearly recite determining masses by mass spectrometry.

Claims 169-173 are rejected under this section for different reason. It is noted that claim 169, step (d) recites "whereby the one or more sequence variations in the target nucleic acid are determined from the candidate sequence variations", and that this step is recited before step (e) (the scoring step). Furthermore, step (e) *also* recites "whereby a sequence variation in the target nucleic acid is determined from the candidate sequence variation scoring in (e)." As an aside, the "in (e)" at the end of step (e) is unnecessary. If the one or more sequence variations are determined in step (d), then what is the meaning of "determined" in step (e)? To recite "whereby the sequence variation is determined" in both steps (d) and (e) is confusing, and this limitation should be removed from step (d), since it is only the scoring step that allows the determination of the sequence variation from among the sequence variation candidates, as discussed in the 112, 1st paragraph rejection above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 74-127, 129-131, 140, 158, 162, 164 and 169-173 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 17-31, 42, 43 and 56-70 of copending Application No. 10/933,611. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the ‘611 application only differ from the instant claims in that they are more specific by way of reciting how the nucleic acid is prepared prior to base-specific fragmentation, mass spec analysis, identification of fragments that differ between the target and reference sequence, generation of compomer witnesses, and scoring sequence variation candidates. Thus the claims of

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the '611 application represent a species which anticipates the more generic claims of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed 05/07/2009 have been fully considered but they are not persuasive. Applicant argued that since the claims were in condition for allowance, and since the '611 application was the later filed of the applications, the rejections should be withdrawn. However, as discussed above, the claims are not in condition for allowance. Therefore the provisional double patenting rejection is maintained.

Allowable Subject Matter

Claims 115 and 117-123 are allowable over the prior art. The closest prior art is either Foote (WO 98/54571) or Zabeau (WO 00/66771), who teach obtaining a sequence by conducting a series of specific cleavage reactions and analyzing by mass spectrometry to determine the actual sequence (using as many different cleavage reactions and mass spectra as needed to ultimately arrive at the sequence). There would have been no apparent reason for any "scoring" of candidate sequences, since these methods were used to actually determine the sequence. Applicant's disclosure presents a "short-cut" whereby less cleavage reactions are needed, and the sequence is inferred from a reduced set of sequence variation candidates by scoring such candidates and selecting the candidate or candidates with the better scores.

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Claims 109-111, 162 and 164 are objected to as being dependent upon a rejected base claim, but would be allowable over the prior art if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/
Examiner, Art Unit 1637